

# EFFECT OF ANTIEPILEPTIC DRUGS ON COGNITIVE FUNCTIONS IN SCHOOL GOING CHILDREN WITH EPILEPSY

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M.D. BRANCH - VII

PEDIATRICS



GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL  
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## **CERTIFICATE**

This is to certify that the dissertation titled "**EFFECT OF ANTIEPILEPTIC DRUGS ON COGNITIVE FUNCTIONS IN SCHOOL GOING CHILDREN WITH EPILEPSY**" is the bonafide original work of **Dr.L.LAKSHMI PRABHA**, in partial fulfillment of the requirements for **M.D., Branch - VII, (Pediatrics)** Examination of the Tamil Nadu Dr.M.G.R. Medical University to be held in March 2008.

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## DECLARATION

I **Dr.L.LAKSHMI PRABHA**, solemnly declare that this dissertation, "**EFFECT OF ANTIEPILEPTIC DRUGS ON COGNITIVE FUNCTIONS IN SCHOOL GOING CHILDREN WITH EPILEPSY**" is a bonafide record of work done by me in the Department of Paediatrics, Institute of Social Pediatrics, Govt. Stanley Medical College and Hospital, Chennai, under the guidance of **Prof.Dr.SUJATHA SRIDHARAN, M.D., D.C.H.**, Director, Institute of Social Pediatrics, Govt. Stanley Medical College and Hospital, Chennai - 600 010.

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Place : Chennai

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## INTRODUCTION

Seizures are common in the pediatric age group and occur in approximately 10% of children and the cumulative life time incidence of epilepsy is 3% and more than half of cases begin in Childhood<sup>1</sup>.

Epilepsy is a chronic disorder that significantly affects the cognition and behaviour. Ongoing seizures and effect of antiepileptic drugs adversely affect the developing brain. The effect of antiepileptic drugs is double edged in this setting. They may reduce the seizure burden and thus improve the cognitive function<sup>2</sup>.

Cognitive function and behaviour have been areas of special interest as these are closely related to academic achievement and development of a healthy and useful personality.

It has been observed that even with normal intelligence children with epilepsy are more likely to fail academically and show increased behavioural problems when compared not only with normal healthy children but also with children having other chronic disorders<sup>3,4</sup>.

In our Department of Pediatric Neuromedicine, there are large number of children with seizure disorder receiving antiepileptics for years.

There is paucity of data regarding the cognitive functions and epilepsy in our country, which will be useful in management of the educational aspect of epileptic children.

With this background it is decided to conduct a study to assess the cognitive functions of the above children in context with individual lobar assessment of brain.

## **AIM OF THE STUDY**

1. To assess the cognitive function in school going children with epilepsy who are all on antiepileptic drugs.
2. To find the prevalence of cognitive dysfunction in children on antiepileptic drugs with epilepsy.
3. To analyse the risk factors associated with cognitive dysfunction.



## **MATERIALS AND METHODS**

Study design : Retrospective Study

Study place : Pediatric Neuromedicine Department, Institute of Social Pediatrics.  
Stanley Medical College and Hospital

Study duration : 2 years, From Sep. 2005 to Sep. 2007

Sample size : 45

### **SUBJECTS**

Children receiving antiepileptic drugs from outpatient Department of Pediatric neurology are selected applying the inclusion and exclusion criterias.

#### **Inclusion Criteria**

1. Children of 7 - 12 years.
2. On antiepileptic drugs atleast for 1 year with good compliance.
3. Normal CT brain
4. Good Academic Performance before the onset of seizures.

#### **Exclusion Criteria**

1. Cerebral Palsy with seizure disorder
2. Mental retardation with seizure disorder
3. Seizures with focal neurological deficit
4. Abnormal CT brain

## **METHODOLOGY**

The study subjects were 45 school going epileptic children selected based on the inclusion criteria from those attending our pediatric neurology OPD for followup and medication who were fully investigated.

After initial evaluation, the children were subjected to various tests to assess each of the specific neuropsychological functions such as motor and speech functions, visuospatial functions, executive functions, learning and memory functions using. **NIMHANS NEUROPSYCHOLOGICAL BATTERY FOR CHILDREN.**

## **DESCRIPTION OF THE BATTERY**

- \* Each test is a measure of a known specific neuropsychological function.
- \* The construct validity of each test is well established.
- \* Tests are age appropriate.
- \* Normative percentile for each test is given according to the sex and age.
- \* Test examine the functions of frontal, parieto - occipital, and temporal lobes.

## NIMHANS NEUROPSYCHOLOGICAL FUNCTION TEST

Lobes	Functions	Tests
FRONTAL LOBE	Motor Functions	
	Motor Speed	Finger tapping test. Right/Left <sup>13</sup>
	Motor Coordination	Hand tapping Right / Left <sup>14</sup>
	Attention	
	Sustained attention	Colour cancellation Test <sup>15</sup>
	Focused attention	Colour Trails Test, Trail A & B <sup>16</sup>
	Expressive speech	
	Repetitive speech	Repeating sounds Repeating words
	Nominative speech	Categorical naming
	Narrative speech	Sentence construction <sup>14</sup>
	Verbal working memory	N back test (1 back /2 back)
	Visuospatial working memory	N back test (VSMW) (1 back/2 back)

Lobes	Functions	Tests
PARIETAL LOBE	Visuoperceptual ability	Motor Free Visual perception Test (MVPT)
	Visuoconceptual ability	Picutre completion Test (PCT) (MISIC, 1969)
	Calculation	Age appropriate sums
	Reading, Writing	Age appropriate paras
TEMPORAL LOBE	Verbal Comprehension	Token Test (DE Rnzi & Vignolo, 1962)

## **DESCRIPTION OF THE TESTS**

### **1. Motor Speed : Finger Tapping Test (Spreen and Strauss, 1998)<sup>17</sup>**

#### **Rationale**

Finger Tapping Test is a measure of motor speed. This test has been found to be sensitive to the presence and laterality of brain lesion (Bigler and Tucker, 1981).

#### **Material**

Finger tapping instrument, stopwatch

#### **Description**

Finger Tapping Test consists of an especially adopted electric finger - tapping instrument. The subject is asked to tap the mounting key as rapidly as possible using the index finger of the preferred hand. A comparable set of measurements is then obtained with the non - preferred hand. Fatigue may affect performance, so a brief rest period of 30 seconds is given after the 3rd trial. A practice trial is given before the test begins. Finalyson and Reitan (1976) gave normative data for right - handed boys and girls in the age range of 6 to 14 years.

Scoring : The mean number of taps on five consecutive trials comprises the score for each hand separately.

## **2. Motor Coordination : Hand Tapping (Luria, 1973)<sup>18</sup>**

### **Rationale**

Hand Tapping Test is a measure of motor coordination.

### **Description**

This test is conceptually based on Luria's description of the use of hand tapping for the assessment of motor coordination. Hand Tapping Test of motor coordination consists of five different sequences tapped by the examiner one by one. These sequences are predetermined and include sequences alternating between the two hands. The subject should be seated across the table. The examiner is required to tap one sequence at a time and the subject is required to repeat the sequence tapped. The examiner should not verbally narrate the sequence. The subject is required to follow the sequence and then tap the same.

1. 2 right 1 left, 2 right 1 left
2. 3 right 2 left, 3 right 2 left
3. 2 left 3 right, 2 left 3 right
4. 3 left 2 right, 3 left 2 right

### **Scoring**

Performance on this test does not yield a quantitative score. Performance is evaluation in terms of fair or poor motor coordination depending on the number of sequences tapped correctly.

### 3. **Sustained Attention : Color Cancellation Test (Kapur, 1974)<sup>15</sup>**

#### **Rationale**

Color Cancellation Test is a measure of sustained attention. It is also a measure of accurate visual scanning, activation and inhibition of a rapid response. More number of omissions reflects poor visual scanning and poor selective attention. More number of commissions reflects problems in inhibition of a rapid response.

#### **Material**

Colour cancellation sheet, pencil and stopwatch.

#### **Description**

The subject is presented with a sheet having 150 circles in 5 different colors i.e. red, yellow, blue, black and gray. Subject is required to cancel only the red and yellow circles as fast as possible. Time taken to complete the test is recorded and errors of omissions and commissions are noted.

#### **Instructions**

This is a sheet having circles in 5 different colors. I want you to cancel only the red and yellow circles in the whole sheet as fast as you can".

Scoring : Time taken in seconds and errors of omission and commission comprise the score.

#### **4. Focused Attention : Color Trails Test (D' Elia, Satz, Uchiyama & White, 1996)<sup>16</sup>**

##### **Rationale**

Color Trails Test is a measure of focused attention. It is also a measure of mental or conceptual tracking and cognitive flexibility. Trail Making Test has been found to be highly sensitive to brain damage (O'Donnel, 1983).

##### **Material**

Colour trial sample sheets, colour trails A and B, stopwatch.

##### **Description**

Color trails test (D'Elia et al., 1996) has been included in the present battery because of its wider applicability. This test is designed to minimize the influence of language and covers a wide age range from childhood to adulthood. It has two parts, 'Part A' and 'Part B'. On 'Trail A' circles numbered 1 to 25 are in two colors yellow and pink. All odd numbered circles are in pink and even numbered circles in yellow. The subject is required to serially connect the numbers 1 to 25, irrespective of the colors. 'Trail B' shows all numbers from 1 to 25 twice in pink and in yellow. The subject is required to connect the numbers serially from 1 to 25 alternating between pink and yellow circles and disregarding the numbers in circles of the alternate color. Time taken for both trial A and B are noted separately. Errors are also recorded.

##### **Scoring**

Time taken in seconds and errors of omissions and commissions for 'Trail A' and 'Trail B' separately comprise the score for this test.

## **5. Expressive Speech**

### **Rationale**

Three components of expressive speech were included in the assessment.

1. Repetitive speech
2. Nominative speech
3. Narrative speech

### **Description**

The items of repetitive, nominative and narrative speech were developed by the authors conceptually based on Luria's description of the assessment of expressive speech (Luria, 1973).

### **Repetitive Speech**

The subject is asked to repeat an increasing series of 3 and 4, simple sounds and words. A set of 3 and 4 sounds and a set of 3 and 4 words are given. A score of '1' is given for a correct repetition of each set. Maximum score on this test is '4'.

### **Nominative Speech**

Assessment of nominative speech consists of object naming, categorical naming and naming through description. For object naming, subject is presented with a sheet with 10 - pictured objects and the subject is asked to name any five objects out of the 10 objects printed on the sheet. This test is also used to rule out visual object agnosia. For categorical naming the subject is presented with a set 5 words, which belong to one category for example, spoon, plate, glass - utensils. 10 such items of 5 words are given. Subject has to give one word, which defines all the words in each item. Lastly the subject is presented with a simple description and is asked to name what it is such as, "What is it which tells time". Five such items are given. Each correct item is given a score of '1'.



## **Narrative Speech**

Subject is given 3 words and asked to construct simple sentence using all the three words in one sentence. Three such sets are given. A score of '2' is given for each correct sentence construction. Maximum score obtained on this test is '6'.

## **Scoring**

A summated score is obtained adding the scores of items of Repetitive speech, Nominative speech and Narrative speech. Maximum total score obtained on Expressive speech is '30'.

## **6. Verbal Working Memory : N Back Task (Smith and Jonides, 1995)<sup>19</sup>.**

### **Rationale**

N back Task (verbal) is a measure of verbal working memory. N back Task has been used to assess verbal working memory. PET studies have revealed two major sites of activation in the N back Task particularly the '2 back' verbal working memory task : Activation is observed in the posterior parietal cortex in the left hemisphere which is thought to be responsible for storage of verbal material. The other sites of activations are a trio of locations in the prefrontal cortex : these are in the inferior frontal gyrus, posterior to this in premotor cortex, and in the supplementary motor area. These activations primarily mediate the production of internal speech code required for rehearsal (Smith and Jonides, 1995).

### **Material**

List of phonemes and record form

### **Description**

Each phoneme is presented at the rate of one phoneme per second.

### **Instructions**

### **1 back Task**

"I will be reading out a list of sounds such as ga, na, ja. As each sound appears, you have to decide whether or not it matched the sound that appeared just before the present sound. If so, I want you to say 'Yes' otherwise say 'No'. Listen carefully".

### **2 back Task**

"Again, I will be reading out sounds such as ga, ma, pa. As each sound appears you have to decide whether it matched the sound that appeared two items / sounds back in the sequence. I want you to say 'Yes' if it is so, otherwise say 'No'.

### **Scoring**

The N back task (verbal) obtains 2 scores. One score is called a hit that is the number of correct responses. The other score is called misses that is scored when the subject has missed a correct target and said 'No' for a phoneme when he should have said 'Yes'. Each of the two scores are obtained separately for the '1 back' and '2 back' tasks.

## **7. N back Task of Visuospatial Working Memory (Smith and Jonides, 1995)<sup>19</sup>**

### **Material**

36 cards for 1 back task, 36 cards for 2 back task and record form.

### **Description**

N back Task (visuospatial) of visuospatial working memory measures storage, manipulation and rehearsal of spatial information. It consists of a '1 back Task' and a '2 back task'. '1 back task' consists of a set of 36 cards. Each card has one dot on it. Dots are placed on spatially different locations on each of these cards in an imaginary circle. The cards are

successively placed on the table in the same location. Each card is presented at the rate of 2 seconds per card. As each card is presented the subject has to decide whether the location of the dot in the present card matches with the location of the dot in the card, which appeared just before the present card. If so the subject has to say 'Yes' otherwise say 'No'. The '2 back Task' also consists of a set of 36 cards. As each card is presented, the subject has to decide whether or not the location of the dot in the present card matches with the location of the dot, which appeared two cards before the present card. If so the subject has to say 'Yes' otherwise say 'No'. The target stimulus items are the ones with underlined card numbers in the record form.

## **8. Visuo - Perceptual Ability : Motor - Free Visual Perception Test (Collaruso & Hammill, 1972)<sup>20</sup>**

### **Rationale**

Motor - Free Visual Perception Test (MVPT) is a test of visual perception, which avoids motor involvement and which is practical for screening, diagnostic and research purposes. This test is a measure of visuoperceptual ability in terms of spatial relationships, visual discrimination, figure ground, visual closure and visual memory.

### **Material**

Set A : 36 items (5 - 8 years)

Set B : 36 items (9 - 12 years)

### **Description**

The original version of MVPT consists of 36 items developed for the 5-12 year old children. It is a 36 - item individually administered, multiple - choice test of visual perception. One stimulus item is presented and the subject is required to respond in terms of making a

correct choice from the 4 response options given. The nature of stimulus items and the 4 response options vary with respect to the different theoretical constructs of visual perception. The test items consist of line drawings, abstract designs, patterns or figures. These 36 items include items on spatial relationships, visual discrimination, figure ground perception, visual closure and visual memory. These five categories are the most prominent theoretical constructs of visual perception.

**Spatial relationship :** This involves the ability to orient one's body in space and to perceive the positions of objects in relation to one - self and to other objects. An example of a spatial relationship task would be the perception of pictures, figures or patterns, which are disoriented in relation to each other (for example, reversals).

**Visual discrimination :** This is the ability to discriminate dominant features in different objects i.e., to discriminate position, shapes, forms and colors and letter like forms.

**Figure ground :** The ability to distinguish an object from its background.

**Visual closure :** The ability to identify complete figures when only fragments are presented.

**Visual memory :** The ability to recall dominant features of one stimulus item.

## **9. Visuo - Conceptual Ability : Picture Completion Test (MISIC, 1969)<sup>21</sup>**

### **Rationale**

Picture Completion Test is a measure of visuo - conceptual ability, visual organisation and visuo - conceptual reasoning. It also elicits concrete thinking (Lezak, 1995).

**Material**

20 cards with incomplete pictures and record form

**Description**

Picture Completion Test is a subtest in Weschler's intelligence scale (WISC - R) for children. The picture completion test included in the present battery has been taken from Malin's intelligence scale for children (Malin, 1969), an Indian adaptation of WISC. Picture completion test consists of 20 cards, each of which has incomplete pictures of human features, familiar objects or scenes arranged in order of difficulty. The examiner presents each card for 15 seconds. The subject is required to point out the missing part in each card as it is presented. Test is discontinued after four consecutive failures.

Score : Number of correct responses comprises the raw score.

**10. Writing : Writing to Dictation and Copying****Material**

10 words for dictation, a passage for copying

**Description**

Age appropriate 10 words are given for dictation. A passage is given for copying. Errors in dictation and copying are recorded in terms of ignoring punctuation marks, spelling errors, adding / missing out or substituting letters / words. (The 10 words for dictation and a passage for copying can be taken with respect to the child's educational level).

**Scoring**

Number of correct words written to dictation comprises the score for dictation. A maximum score of 10 for dictation and score of 10 for a passage copied correctly was given.

Maximum score obtained on the writing test is 20.

## **11. Calculation**

Duration : Age Appropriate Additions, Subtraction, Multiplication and Knowledge of tables.

### **Rationale**

Basic calculation skills are assessed in terms of simple and graded additions, subtraction, multiplication and knowledge of tables to assess age appropriate normal levels of calculation skills to rule out dyscalculia in the clinical sample. (Burbaud et al., 1999)<sup>22</sup>.

### **Description**

Age appropriate sums of simple and graded addition, subtraction, multiplication and tables are given to assess basic calculation skills.

Scoring : Number of correct solutions comprises the score. Maximum score obtained is 20.

## **12. Verbal Comprehension : Token Test (De Renzi & Vignolo, 1962)<sup>23</sup>**

### **Rationale**

Token test is a measure of verbal comprehension of commands of increasing complexity (Spreeen and Strauss, 1998)<sup>17</sup>

### **Material**

20 tokens in 5 colours (red, white, yellow, blue and green), 2 sizes (small - 2 cm in diameter and large - 3 cm in diameter) and 2 shapes (circle and square); 36 commands.

### **Administration and Instructions**

The tokens are placed in front of the subject from left to right with reference to the subjects side in a fixed order given below :

**Row 1**

Large circles in order : red, blue, yellow, white and green

**Row 2**

Large squares in order : blue, red, white, green and yellow

**Row 3**

Small circles in order : white, blue, yellow, red and green

**Row 4**

Small circles in order : yellow, green, red, blue and white

The list of 36 commands is split into 6 sections : section A to f. Commands can be repeated once. The commands are given clearly and slowly. Before starting with the commands the tokens are placed in front of the subject from left to right from the subject's side. Following instructions are given to introduce the test :

"Here are some tokens in five different colors, 2 shapes and 2 sizes. I will be giving some instructions to you one by one and I want you to carry them out using these tokens. Listen carefully and do as I say. Do as much as you remember". The text is discontinued after 3 consecutive failures.

**Scoring**

One point is given for each correctly performed item. For each repeated instruction a score of  $\frac{1}{2}$  is given instead of 1. Maximum score obtained on this test is 36.

## REVIEW OF LITERATURE

Seizure : A Seizure or convulsion is a paroxysmal, time limited change in motor activity and / or behaviour that results from abnormal electrical activity in the brain.

Seizures are common in the pediatric age group and occur in approximately 10% of children. Most seizures are provoked by somatic disorders originating outside the brain, such as high fever, infection, syncope, head trauma, hypoxia, toxins or cardiac arrhythmias<sup>1</sup>.

Epilepsy : A condition in which seizures are triggered recurrently from within the brain.

Less than one third of seizures in children are caused by epilepsy.

**For epidemiologic classification purposes epilepsy is considered to be present when two or more unprovoked seizures occur at an interval greater than 24 hrs apart<sup>1</sup>.**

The cumulative life time incidence of epilepsy is 3% and more than half of cases begin childhood.



## INTERNATIONAL LEAGUE AGAINST EPILEPSY- CLASSIFICATION

### **Partial Seizures**

Simple partial (consciousness retained)

Motor

Sensory

Autonomic

Psychic

Complex partial (Consciousness impaired)

Partial seizures with secondary generalization

### **Generalized seizures**

Absence

Typical

Atypical

Generalized tonic - clonic

Tonic

Clonic

Myoclonic

Atonic

Infantile spasms

### **Unclassified seizures**

## **PARTIAL SEIZURES**

### **Simple partial seizures**

Motor activity is the most common symptom of simple partial seizures. The movements are characterised by asynchronous clonic or tonic movements and they tend to involve the face, neck and extremities.

Automatism do not occur with simple partial seizure.

Patient remains conscious and may verbalize during the seizure<sup>1</sup>.

### **Complex partial seizures**

It may begin with a simple partial seizure with or without an aura, followed by impaired consciousness; conversely, the onset of the complex partial seizure may coincide with an altered state of consciousness.

An aura consisting of vague, unpleasant feelings, epigastric discomfort or fear is present in approximately one third of children with simple partial seizures and complex partial seizures.

Impaired consciousness in infants and children is difficult to appreciate. There may be a brief blank stare or a sudden cessation or pause in activity that is frequently over looked by the parent.

Automatisms occurs in 50 - 75% of cases<sup>1</sup>.

## **GENERALIZED SEIZURES**

### **Absence Seizures**

Simple (typical) absence (petit mal) seizures are characterized by a sudden cessation of motor activity or speech with a blank facial expression and flickering of the eyelids.

- \* Uncommon before age 5 years
- \* More common in girls
- \* Never associated with aura
- \* Rarely persist longer than 30 sec.
- \* Not associated with a postictal state.

## **GENERALIZED TONIC - CLONIC SEIZURES**

These seizures are extremely common and may follow a partial seizure with a focal onset (Secondary generalization) or occur de novo.

They may be associated with an aura, suggesting a focal origin of the epileptiform discharge.

The clonic phase of the seizure is heralded by rhythmic clonic contractions alternating with relaxation of all muscle groups.

Loss of sphincter control, particularly the bladder is common during a generalized tonic - clonic seizure<sup>1</sup>.

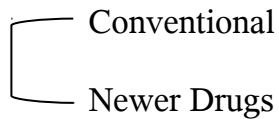
## MYOCLONIC EPILEPSIES OF CHILDHOOD

It is characterized by repetitive seizures consisting of brief, often symmetric muscular contractions with loss of body tone and falling or slumping forward, which has a tendency to cause injuries to the face and mouth<sup>1</sup>.

It includes

1. Benign myoclonus of infancy
2. Typical myoclonic epilepsy of early childhood
3. Complex myoclonic epilepsy
4. Juvenile myoclonic epilepsy (Janz syndrome)
5. Progressive myoclonic epilepsies

## ANTI EPILEPTIC MEDICATIONS



### I. Conventional Drugs

#### 1. Phenobarbitone :

Mechanism of Action : Enhances GABA transmission and modulates channels.

Pharmacokinetics : It is :

\* 50% protein bound

\* Metabolized in Liver

\*  $t_{1/2}$  is 60 hrs (Shorter in children)

\* Steady state reached after 4 wks of drug initiation.

Indications : Partial onset and generalized seizures

Dose : 4-6 mg/kg /day in older children.

Side effects

Changes in behaviour, affect and cognition in upto 50% of patients. Hyperactivity and sleep disturbances are common<sup>5</sup>.

## PHENYTOIN

Mechanism of Action : Stabilizes voltage - dependent sodium channels.

Pharmacokinetics : Strongly protein bound metabolized in the liver  $t_{1/2}$  is 13 hours.

Indications : Partial seizures and GTCs

(I.V) Status epilepticus

Dose : 3-8 mg/kg/day (maintenance)

Side effects : Unsteadiness, cerebellar ataxia, lymphadenopathy, gum hypertrophy, folic acid and Vit D deficiency.

Mental slowness on long term treatment.

## SODIUM VALPROATE

Mechanism of Action : Unknown, possibilities include increasing GABA levels or an action on  $K^+$  channels.

Pharmacokinetics : Strongly protein bound.  $t_{1/2}$  is 12 hrs.

Indications : All seizure types

Dose : Start as 10mg / kg / day  
maintenance dose can upto 20-30 mg/kg/day

Side effects : Hairloss,  
Hyperammonaemia secondary to occult ureacycle disorders, Hepatotoxicity<sup>5,6</sup>.

## CARBAMAZEPINE

Mechanism of Action : Stabilizes voltage - dependent sodium channels.

Pharmacokinetics : Strongly protein bound

Highly lipid soluble

Oxidized by the Liver P 450 enzyme

t<sub>1/2</sub> is 5-24 hrs while on maintenance

Indications : Partial onset / GTCS

Dose : 5mg/kg/day  
maintenance 10-30mg / kg / day

Side effects : Allergic neutropenia, unsteadiness, No known serious long term side effects<sup>5,6</sup>.

## Benzodiazepines

\* Potentiate GABA receptor activity

Mild antiepileptic

Causes sedation<sup>5</sup>

## **NEWER DRUGS**

Gabapentin, Oxcarbazepine, Tiagabine,

Lamotrigine, Topiramate, Vigabatrin

Levetiracetam, Felbamate, Remacemide,

Zonisamide, Losigamone<sup>7</sup>.

## **COGNITIVE OR NEUROPSYCHOLOGICAL FUNCTIONS OF BRAIN**

- Frontal Lobe : 1. Motor Functions  
Motor speed  
Motor co-ordination
2. Attention  
Sustained attention  
Focused attention
3. Speech  
Expressive speech  
Repetitive speech  
Nominative speech  
Narrative speech
4. Executive functions  
a. Verbal fluency  
b. Design fluency  
c. Verbal working memory  
d. Visuospatial working memory  
e. Planning

## **II. PARIETAL LOBE**

- a. Visuo - perceptual ability  
b. Visuo - conceptual ability  
c. Visuo - constructive ability  
d. Visual recognition

- e. Somatosensory perception
- f. Tactile finger localization
- g. Tactile form perception
- h. Reading
- i. Writing
- j. Calculation

### III. TEMPORAL LOBE

- a. Verbal comprehension
- b. Verbal learning and memory
- c. Visual learning and memory

Impairment of cognitive functions and behaviour are important problems in children with epilepsy.

The reasons for the cognitive impairment are multifactorial but besides primary brain pathology, certain factors like age at onset of seizure, seizure type and antiepileptic drugs (AEDs) have been observed to be closely associated with **cognitive dysfunction and behavioural disturbances, although it is often difficult to determine the relative contribution of any given factor** - as emphasized by Mitchel et al., 1991<sup>8</sup>.

Further seidenberg et al., 1986, says Attention, concentration and memory are important areas of cognitive dysfunction in epileptic children which their perform a vital role in academic under achievement<sup>9</sup>.

About 16-50% of epileptic children have been reported to be academic under achievers due to various cognitive dysfunction - as emphasized by Mitchel et al., 1991<sup>8</sup>.



A.P.Aldenkamp, Alpherts et al., *Epilepsia*., 39(10), 1070 - 1074, 1998 in their study on Antiepileptic Drug - Related cognitive complaints in seizure - free children with epilepsy before and after drug discontinuation, found that, significant improvement in memory, concentration, attention, alertness after discontinuation of antiepileptic drugs for >1 yr<sup>10</sup>.

Further Jane Williams, Stephen Bates et al., *Epilepsia J*, 1998 in their study found that Short term (6 months) antiepileptic drug treatment in children does not adversely affect the cognitive function and behaviour of the children<sup>11</sup>.

Pratibha D. Singhi, Usha Bansal, et al., PGI, Chandigarh also noticed Low IQ profile in children with Idiopathic Generalized Epilepsy<sup>12</sup>.

## RESULTS AND OBSERVATION

**TABLE - 1a**

***TEST FOR FRONTAL LOBE***

Sl.No.	Test S.No.	Normal	Abnormal
1.	FTT-R	39 (86.7%)	6 (13.3%)
2.	FTT-L	39 (86.7%)	6 (13.3%)
3.	HT	43 (95.6%)	2 (4.4%)
4.	CCT	39 (86.7%)	6 (13.3%)
5.	CTA	39 (86.7%)	6 (13.3%)
6.	CTB	39 (86.7%)	6 (13.3%)
7.	SPSC*	43 (97.7%)	1 (2.3%)
8.	NBT <sub>1</sub>	39 (86.7%)	6 (13.3%)
9.	NBT <sub>2</sub>	39 (86.7%)	6 (13.3%)
10.	VSNBT <sub>1</sub>	39 (86.7%)	6 (13.3%)
11.	VSNBT <sub>2</sub>	39 (86.7%)	6 (13.3%)

### ABBREVIATIONS ATTACHED IN THE ANNEXURE

Out of the 45 children analyzed for frontal lobe function using NIMHANS Neuropsychological Battery for children, 6 children exhibit impaired frontal lobe function.

On applying the above battery, it is observed that there is significant reduction in the motor speed both Right and left depicted by finger tapping test (<5<sup>th</sup> percentile).

\* Out of 45, one child is not applicable for speech score as he falls exactly on 7 years (> 7 years in must for speech score).

Significant impairment is observed with attention both sustained and focused.

Regarding speech score—Narrative speech is affected more than the Repetitive and Nominative speech. As such speech is affected less.

Regarding the Executive functions design fluency, verbal working memory and Visuospatial working memory were significantly impaired (<5<sup>th</sup> percentile).

Further it is observed that more than 65% of the children analyzed have scored low normal range of normative value for their age and sex (<10<sup>th</sup> percentile).

**TABLE - 1b**  
***FRONTAL LOBE FUNCTIONS***

S. No.	Functions	Total	Normal	Abnormal
1.	Motor speed	45	39 (86.7%)	6 (13.3%)
2.	Attention Sustained Focused	45	39 (86.7%)	6 (13.3%)
3.	Speech	44	43 (95.6%)	1 (2.2%)
4.	Verbal working memory	45	39 (86.7%)	6 (13.3%)
5.	Visuospatial working memory	45	39 (86.7%)	6 (13.3%)

It is observed that 1 out 8 children examined is affected with decline in motor speed, Attention, verbal and Visuo spatial working memory.

1 out 22 children examined is affected with speech.

**TABLE - 2a**  
***TEST FOR PARIETAL LOBE FUNCTION***

	Normal	Abnormal
MVPT	43 (95.6%)	2 (4.4%)
PCT	43 (95.6%)	2 (4.4%)
Writing	43 (95.6%)	2 (4.4%)
Calculation	45 (97.8%)	1 (2.2%)

Out of the 45 children analyzed, 2 children were found to have parietal lobe dysfunction. They showed significantly low score in their,

Visuoperceptual ability

Visuo conceptual ability

Visual recognition

Writing

Calculation

Around 25% of the children showed low normal range of normative value for their age and sex.

**TABLE - 2b**  
***FUNCTION OF PARIETAL LOBE AFFECTED***

<b>S. No.</b>	<b>Functions</b>	<b>Total</b>	<b>Normal</b>	<b>Abnormal</b>
1.	Visuo perception	45	43	2
2.	Visuo conception	45	43	2
3.	Writing	45	43	2
4.	Calculation	45	44	1

**TABLE - 3**  
***TEST FOR TEMPORAL LOBE FUNCTION***

<b>Test</b>	<b>Normal</b>	<b>Abnormal</b>
TT	45 (100%)	0 (0.0%)

We also observed that all the children have normal temporal lobe function with respect to verbal comprehension depicted by token test.

**TABLE - 4****PREVALENCE OF COGNITIVE IMPAIRMENT**

	<b>Total</b>	<b>Normal</b>	<b>Abnormal</b>
Cognitive impairment  (Frontal & Parietal)	45	39 (87.0%)	6 (13.0%)

The prevalence of cognitive impairment was found to be 13% in our study.

**DEMOGRAPHIC PROFILE OF COGNITIVE FUNCTION IN****A CHILD WITH EPILEPSY****TABLE - 5****AGE GROUP VS COGNITIVE IMPAIRMENT**

Age Group	Status					<i>Significance</i>  <i>e</i>
	<i>Total</i>	Normal		Abnormal		
		N	%	N	%	
7-9 yrs	20	18	90%	2	10%	$\chi^2 = 0.34$  p = 0.56
10-12 yrs	25	21	84%	4	16%	Not significant

Total number of children in the present study is 45. Out of which 7-9 yrs are 20. Among the 20 cognitive dysfunction were found in 2 (10%) children.

10-12 yrs are 25. Among the 25 cognitive dysfunction were found in 4 (16%) children.

P value is 0.56, statistically not significant.

TABLE - 6

SEX DISTRIBUTION Vs COGNITIVE IMPAIRMENT

Sex	Status					<i>Significance</i>
	<i>Total</i>	Normal		Abnormal		
		N	%	N	%	
Male	25	22	88%	3	12%	$\chi^2 = 0.09$ p = 0.77
Female	20	17	85%	3	15%	Not significant

Out of the 25 males children analysed with Nimhans. Neuropsychological battery 3 were found to have cognitive dysfunction (12%).

Out of 20 female children analysed with Nimhans Neuropsychological battery 3 were found to have cognitive dysfunction (15%).

P value is 0.77 statistically not significant.

**TABLE - 7**

LITERACY OF FATHER Vs COGNITIVE IMPAIRMENT

Father	Status					Significance
	N	Normal		Abnormal		
	Total	N	%	N	%	
Literate	26	24	92.3%	2	7.7%	$\chi^2 = 1.69$ p = 0.19
Illiterate	19	15	78.9%	4	21.1%	Not significant

Out study shows out of 26 children of Literate fathers, 2 children were found to have cognitive dysfunction (7.7%).

Out of 19 children of illiterate father, 4 were found to have cognitive dysfunction (21.1%).

P value is 0.19, statistically not significant.

**TABLE - 8**

LITERACY OF MOTHER

Mother	Status					<i>Significance</i>
	N	Normal		Abnormal		
	<i>Total</i>	N	%	N	%	
Literate	19	17	89.5%	2	10.5%	$\chi^2 = 0.22$ p = 0.64
Illiterate	26	22	84.6%	4	15.4%	Not significant

The above table shows out of 19 children of Literate mothers, 2 children were found to have decline in cognitive function (10.5%).

Out of 26 children of illiterate mothers, 4 were found to have decline in cognitive function (15.4%).

P value is 0.64, statistically not significant.

**TABLE - 9****AGE AT ONSET OF SEIZURES**

Age at Onset of seizures	Status					<i>Significance</i>
	N	Normal		Abnormal		
	<i>Total</i>	N	%	N	%	
<6 Yrs	19	17	89.5%	2	10.5%	$\chi^2 = 0.22$ p = 0.64
> 6 Yrs	26	22	84.6%	4	15.4%	Not significant

In our study group the total number of children with age at onset of seizures below 6 yrs were 19 out of which 2 showed decline in cognitive function (10.5%).

Age at onset of seizures above 6 yrs. Of age were 26, out of which 4 showed decline in cognitive function (15.4%).

The P value is 0.64, statistically not significant.

**TABLE - 10****TYPE OF SEIZURES**

Type of seizures	Status					<i>Significance</i>
	Total	Normal		Abnormal		
		N	%	N	%	
GTCS	27	23	85.2%	4	14.8%	$\chi^2 = 5.13$ p = 0.16
Focal	10	10	100%	-	-	
Complex partial	5	3	60%	2	40%	Not significant
Simple partial	3	3	100%	-	-	

Out of the 45 children analysed. Generalized Tonic clonic seizures was found to be in 27 children, among those 4 were found to have cognitive decline (14.8%).

Focal seizures are found to present in 10 out of 45 and the neuropsychological test were



found to be normal in all those children with focal seizures.

Complex partial seizures was found to present in 5 out of 45 and cognitive decline was present in about 2 children (40.0%).

Simple partial seizures was found to present in 3 out of 45 and the neuropsychological battery test were found to be normal in all those children with simple partial seizures.

P value is 0.16, statistically not significant.

**TABLE - 11a**  
POLYTHERAPY Vs MONOTHERAPY

	Status					<i>Significance</i>
	Total	Normal		Abnormal		
		N	%	N	%	
Polytherapy	19	14	73.7%	5	22.7%	$\chi^2 = 4.79$  p = 0.03
Monotherapy	26	25	95.7%	1	4.3%	<b>Significant</b> <b>(p&lt;0.05)</b>

The study shows,

Out of 45 children with epilepsy, 26 children were started with monotherapy and 19 children with polytherapy (>1 drug).

Out of the 19 children with polytherapy 5 children developed decline in the cognitive function (22.7%).

Out of the 26 children with monotherapy only are developed decline in the cognitive

function (4.3%).

P value is 0.03, statistically significant.

**TABLE - 11b**

**DRUG COMBINATIONS IN POLYTHERAPY**

<b>Drug combination</b>	<b>Total</b>	<b>Normal cognition</b>	<b>Cognitive Decline</b>
On Polytherapy	19	14 (73%)	5 (27%)
PBT+PHT only	11	8 (73%)	3 (27%)
PBT+PHT+3 <sup>rd</sup> drug	7	5 (71%)	2 (29%)
Other (CBZ + SVP)	1	1(100%)	-

**ABBREVIATIONS ATTACHED TO THE ANNEXURE**

**TABLE - 12**  
***PHENOBARBITONE***

Phenobarbitone	Status					Significance
	Total	Normal		Abnormal		
		N	%	N	%	
Yes	23	17	73.9%	6	26.1%	$\chi^2 = 6.62$ p = 0.01
No	22	22	100%	-	0%	Significant (P<0.05)

Yes - Taken

No - Not Taken

Out of the 45 children analysed 23 were found to take phenobarbitone, among the 23, 6 were found to have decline in cognitive function (26.1%).

Out of 22 children, who are not taking phenobarbitone, Neuropsychological test were perfectly normal.

On applying chi-square test  $\chi^2$  in 6.62, P value is 0.1, Statistically Significant.

**TABLE - 13**  
***PHENYTOIN***

Phenytoin	Status					<i>Significance</i>
	Total	Normal		Abnormal		
		N	%	N	%	
Yes	24	19	79.2%	5	20.8%	$\chi^2 = 2.50$ p = 0.11
No	21	20	95.2%	1	4.8%	Not significant

Out of the 45 children analyzed, 24 were found to have phenytoin, among the 24, 5 children were found to have decline in cognitive function (20.8%).

Out of 20 children who are all not an phenytoin, only one children showed features of cognitive decline (4.8%).

P value is 0.11, statistically, not significant.

**TABLE - 14**  
***SODIUM VALPROATE***

Sodium valproate	Status					<i>Significance</i>
	<i>Total</i>	Normal		Abnormal		
		N	%	N	%	
Yes	22	21	95.5%	1	4.5%	$\chi^2 = 2.87$ p = 0.09
No	23	18	78.3%	5	21.7%	Not significant

Yes - Taken                      No - Not Taken

Out of the 45 study group children, 22 were found to have Sodium Valproate. Among those children only one demonstrates cognitive dysfunction (4.5%).

Out of 23 children who were not on Sodium Valproate, 5 demonstrates cognitive dysfunction (21.7%).

P value is 0.09 statistically not significant.

**TABLE - 15**

***CARBAMAZEPINE***

Carbamazepine	Status					<i>Significance</i>
	<i>Total</i>	Normal		Abnormal		
		N	%	N	%	
Yes	10	9	90.0%	1	10%	$\chi^2 = 0.12$ p = 0.73
No	35	30	85.7%	5	14.3%	Not significant

Yes - Taken

No - Not Taken

Out of the 45 children analyzed, 10 were found to take carbamazepine, among the 10, only one children was found to have decline in cognitive function (10%).

Out of the 35 children who are not taking carbamazepine, cognitive decline were found in 5 children (14.3%).

P value is 0.73, statistically not significant.

TABLE - 16

***BENZODIAZEPINE***

Benzodiazepine	Status					Significance
	Total	Normal		Abnormal		
		N	%	N	%	
Yes	6	6	100%	-	-	$\chi^2 = 1.06$ p = 0.30
No	39	33	84.6%	6	15.4%	Not significant

Out of the 45 children analyzed, 6 were found to have Benzodiazepine, among the 6, neuropsychological assessment were found to be normal.

P value is 0.30, not significant.

TABLE - 17

***DURATION OF DRUGS***

Duration of drugs	Status					Significance
	Total	Normal		Abnormal		
		N	%	N	%	
1-2 Yrs	23	22	95.7%	1	4.3%	$\chi^2 = 4.56$ p = 0.03
> 2 Yrs	22	17	77.3%	5	22.7%	Significant (P < 0.05)

Out of 23 children who were taking antiepileptic drugs for less than or equal to 2 yrs, only one children showed decline in cognitive function (4.3%).

Out of 22 children who were taking antiepileptic drugs for more than 2 yrs duration with good compliance, 5 children showed decline in cognitive function (22.7%).

Applying chi - square test  $\chi^2$  is 4.56.

**P value is 0.03, statistically significant.**

TABLE - 18

***DOSAGE***

Dosage	Status					Significance
	Total	Normal		Abnormal		
		N	%	N	%	
Normal (Therapeutic range)	40	36	90.0%	4	10.0%	$\chi^2 = 3.46$ p = 0.06
Higher	5	3	60.0%	2	40.0%	Not significant

Out of the 45 children analyzed. 40 children were found to take antiepileptic drugs (both Monotherapy and Polytherapy) with usual dosage. Out of 40, 4 children demonstrates features of cognitive decline (10.0%).

Among the 45, 5 children were found to take higher dose of antiepileptic drugs because of poor seizure control and out of 5, 2 demonstrates features of cognitive decline (40.0%).

P value is 0.06, statistically not significant.

**DEMOGRAPHIC PROFILE / RISK FACTORS OF COGNITIVE FUNCTION IN A CHILD  
WITH EPILEPSY ON ANTIEPILEPTIC DRUGS**

Variables		Total	Status				Significance
			Normal		Abnormal		
			n	%	n	%	
Age	7-9	20	18	90.0%	2	10.0%	$\chi^2=0.34$ P=0.56 Not significant
	10-12	25	21	84.0%	4	16.0%	
Sex	Male	25	22	88.0%	3	12.0%	$\chi^2=0.09$ P=0.77 Not significant
	Female	20	17	85.0%	3	15.0%	
Father	Literate	26	24	92.3%	2	7.7%	$\chi^2=1.69$ P=0.19 Not significant
	Illiterate	19	15	78.9%	4	21.1%	
Mother	Literate	19	17	89.5%	2	10.5%	$\chi^2=0.22$ P=0.64 Not significant
	Illiterate	26	22	84.6%	4	15.4%	
Age of onset of seizure	< 6 yrs	19	17	89.5%	2	10.5%	$\chi^2=0.22$ P=0.64 Not significant
	> 6 yrs	26	22	84.6%	4	15.4%	
Type of seizure	GTCS	27	23	85.2%	4	14.8%	$\chi^2=5.13$ P=0.16 Not significant
	Focal	10	10	100.0 %			
	CPS	3	3	60.0%	2	40.0%	
	SPS	3	3	100.0 %			
Poly therapy& Mono therapy	Mono therapy	26	25	96.2%	1	3.8%	$\chi^2=4.79$ <b>P=0.03</b> <b>significant</b>
	Poly therapy	19	14	73.7%	5	26.3%	
Duration of drugs	1-2 yrs	23	22	95.7%	1	4.3%	$\chi^2=4.56$ <b>P=0.03</b> <b>significant</b>
	2-4 yrs	18	14	77.8%	4	22.2%	
	4-6 yrs	4	3	75.0%	1	25.0%	
Dosage	Yes	40	36	90.0%	4	10.0%	$\chi^2=3.46$ P=0.06 Not significant
	No	5	3	60.0%	2	40.0%	
Phenobarbitone	Yes	23	17	73.9%	6	26.1%	$\chi^2=6.62$ <b>P=0.01</b> <b>significant</b>
	No	22	22	100.0 %			
Phenytoin	Yes	24	19	79.2%	5	20.8%	$\chi^2=2.50$



	No	21	20	95.2%	1	4.8%	P=0.11 Not significant
Sodium valproate	Yes	22	21	95.5%	1	4.5%	$\chi^2=2.87$ P=0.09 Not significant
	No	23	18	78.3%	5	21.7%	
Carbamazepine	Yes	10	9	90.0%	1	10.0%	$\chi^2=0.12$ P=0.73 Not significant
	No	35	30	85.7%	5	14.3%	
Benzodiazepine	Yes	6	6	100.0%			$\chi^2=1.06$ P=0.30 Not significant
	No	39	33	84.6%	6	15.4%	

#### ABBREVIATIONS ATTACHED TO THE ANNEXURE

### RISK FACTORS FOR COGNITIVE DYSFUNCTION

#### MULTI VARIANT ANALYSIS LOGISTIC REGRESSION

Sl.No.	Variables	Sig.	Odds ratio	95.0% C.I.for EXP(B)	
				Lower	Upper
1.	AG SZ	0.716	1.53	.15	15.25
2.	T SZ	0.940	1.04	.37	2.85
3.	P M	0.041	4.69	1.69	14.77
4.	DOD	0.050	1.29	1.17	8.52
5.	DOSE	0.295	4.92	0.24	97.57
6.	PBT	0.351	0.78	0.24	7.57

- \* Odds ratio for polytherapy Vs Monotherapy is 4.69. The relative risk of cognitive dysfunction is 4.69 times when the child is on polytherapy.
- \* Odds ratio for duration of therapy >1 yr. is 1.29.
- \* The relative risk of cognitive dysfunction was found to be 1.29 times if duration of therapy is > 1 yr. (associated with polytherapy).

## DISCUSSION

Attention, concentration and memory are important areas of cognitive function (Frontal lobe) and perform a vital role in academic achievement. About 16-50% of epileptic children have been reported to be academic under achievers due to various cognitive dysfunction (24,25).

They mostly arise from specific cognitive deficiencies rather than generalized cognitive dysfunction.

The present study also confirms impairment of frontal lobe function [specifically attention, memory, concentration, abstract reasoning, information processing] along with parietal lobe function (auditory perceptual abilities, language processing, visuo perception, visuo conception, wiring, calculation) in epileptic children of school going age group (26).

Polytherapy (>1 drug), Duration of Drugs >2 yrs, and Intake of phenobarbitone were associated with significant impairment of all the test parameters of lobar function (frontal and parietal).

And the age at onset of seizures, type of seizures, sex, literacy of mother and father, dosage of drugs, Age at onset of seizures, Phenytoin, Sodium valproate, carbamazepane and Benzodiazepine were not significantly related to the decline in frontal and parietal lobar functions.

### **1. Age group**

Present study shows no co-relation between the age group and cognitive dysfunction. Median age group in 9 yrs.

**K.Jayashree et al. 1999** also not able to observe any specific age group Vs Cognitive dysfunction with epilepsy Median age group in their study in 10 yrs. (24).

## **2. Sex distribution**

Our study shows Male: Female distribution ratio 1:2. No co-relation between gender and cognitive dysfunction were observed.

**Jayashree et al. 1999** observes M: F ratio of 1:6:1 (24).

**Yung-Jung chen et al. 1996** Observes M: F ratio of 1:1 (27).

## **3. Literacy of father**

Present study signifies no co-relation between the cognitive dysfunction and the Literacy of father. Yung-Jung Chen et al. also signifies no co-relation between education, Socio economic status and cognitive impairment.(27).

## **4. Literacy of Mother**

Present study signifies no co-relation between the cognitive dysfunction and the Literacy of Mother.

**Yung-Jung Chen et al.** also signifies no co-relation between education, socio economic status and cognitive impairment (27).

## **5. Age at onset of seizures**

Our study unable to show positive relation between age at onset of seizures and cognitive impairment.

**O' Leary et al. (1983)**<sup>25</sup>

&

**Farwell et al. (1985)** (28) shown impairment of different areas of cognitive function in children with epilepsy in association with early age at onset of seizures.

**Dodril and Troupin et al. (1991)** observed that the longer duration needed for seizure control is frequently associated with early age at onset of seizure (29) and cognitive impairment (26).

**Jayashree et al. (1999)** observed cognitive impairment in cases with age at onset below 5 yrs (24).

## **6. Type of seizures**

Present study observe no consistent relation between type of seizures and cognitive impairment.

**Jayashree et al. 1999** observed that recent memory in cases with simple partial seizures was significantly lower as compared to cases with complex partial and generalized seizure (24).

Present study shows impairment in cognitive function in 2 cases out of 4 with CPS. But the two children were also on polytherapy. We can't isolate whether the cognitive decline is due to polytherapy or complex partial seizures perse.

**Albert Aldenkamp et al. 2004** also observed that there is no consistent relation between the type of seizures and cognitive impairment (30).

**Further (Jayashree et al. 1999, Stores et al. 1981, Ounstead et al. 1966)** signifies impairment of cognition with temporal lobe epilepsy (24).

## **7. Polytherapy Vs Monotherapy**

The present study also confirms that polytherapy significantly impair the cognitive function when compared to monotherapy.

There is considerable evidence that polytherapy in children causes larger number of cognitive dysfunction – **Trimble et al. (1990) (31)**.

**Thompson and Trimble (1982)** observed that the performance task (Reaction time, coding, attention, immediate recognition, memory, perception) were better performed by children on monotherapy when compared to polytherapy (32).

**Jayashree et al. 1999**, observed attention, concentration and all forms of memory were significantly lower in cases of polytherapy compared to monotherapy (24).

**Meador KJM et al. 1990**. Shows polypharmacy had a relatively severe impact on cognitive function when compared with monotherapy irrespective of the type of Antiepileptic drugs used (33).

It is observed that phenobarbitone with phenytoin lowers the cognition significantly when compared to other combinations. When two drugs individually having mild cognitive effect may induce serious cognitive impairment when used in combination(33).

## **8. Duration of drugs**

Our study signifies longer the duration of drug intake more will be the cognitive impairment.

**Jayashree et al. 1999** observed no significant difference amongst the different duration

of drug Categories (24).

**Yung-Jung Chen. et al.** compared cognitive effect of CBZ, PBT, SVP in children with epilepsy using WISC-R, Bender Gestalt test and auditory event-Related potentials (P300) before and 6 and 12 months after AED treatment (27).

He observed no significant difference in the former. It clearly shows that duration of AED significantly affects the cognitive function (ref: Epilepsia J. Vol. 37 No.1, 1996).

## **9. Dosage**

The present study does not signifies any correlation between Dosage and Cognitive dysfunction.

**Sommer field - Zuskind and Zuskind et al. 1940; Aman et al. 1987** reported impairment of cognitive function in association with higher doses of Antiepileptic drugs (34).

**Trimble 1990; Mitchell et al. 1993** also substantiate the above findings in their study (31, 35).

## **10. Phenobarbitone**

Among the antiepileptic drugs analysed, phenobarbitone intake was significantly found to have decline in frontal and parietal lobe function P-value is 0.01.

**Trimble and Corbette et al. (1980)** in their study using the Rutter Behaviour Rating Scale reported that 50% of children receiving Phenobarbitone had some form of conduct disturbance (36).

**Ingram et al. (1986)** noted minimal effects on children of normal intellectual ability without any behavioural disturbances (37).

**Johnston et al. 2004; Gulbati 2003; Lowenstein et al. 2001** also supports the above observation (38, 39).

**Meador KJM et al. 1990** PBT has been shown to have a dramatic impact on cognition when compared to Phenyton, Sodium valproate, Carbamazepine (33).

## **11. Phenytoin**

There are few controlled studies of the effects of phenytoin over cognitive function.

**Vallarta et al. (1974)** reported that progressive encephalopathy may occur, not necessary at toxic drug levels, and often associated with mental retardation (40).

**Trimble and Corbett (1980)<sup>2</sup>** found that serum and red cells folate levels were significantly lower in children reported as neurotic and depressed. And suggested the possibility of a phenytoin related folate deficiency as a cause for the above.

**Gulhati et al. 2003, Lowenstein et al. 2001**, says children showing signs of cognitive deterioration had significantly higher serum phenytoin concentrations than those without such signs (39, 41).

## **12. Sodium valproate**

The present study shows least relation with cognitive function.

**Jeavons et al. 1977 (21)** suggested improvement in mood and alertness with valproate, but general confirmation is still awaited (42).

**Herranz et al. (1982)** reported lassitude, drowsiness, absent mindedness, Sadness and aggression (43).

**Johnston 2004**, reported that it rarely induces behavioural changes (38) **Herranz et al. (1982)** further suggest co-relation between serum level of Valporate with subsequent cognitive dysfunction (43).



### 13. Carbamazepine

There have been favourable reports on the effect of carbamazepine on cognitive function – **Silversten et al. 1982, Schain et al. 1977** (44, 45).

**Schain et al. 1977**-Withdrew barbiturates and substituted carbamazepine in a group of children and reported improved attentiveness and alertness 4-6 months after the introduction of carbamazepine.

**Johnston, 2004, Gulhatl, 2003, Lowenstein et al. 2001**, reported mild confusion drowsiness which may affect the performance of the child (38, 39, 41).

**Thompson and Trimble (1982)** favours the use of carbamazepine in children with cognitive impairment with epilepsy (32). **Rijke vorsel-Harmant et al.** reported no significant change in the cognition with respect to CBZ (46).

### 14. Benzodiazepine

The present study observer there is no consistent relation between BZD and cognitive function.

There are very few controlled studies of the effects of Benzodiazepine and cognitive function.

**Herraz et al. (1982)** reported decreased alertness, drowsiness, increased sleepiness following diazepam intake (43).

## **15. Frontal lobe function test**

It is surprised to observe that even motor speed of the children were also significantly impaired along with memory, sustained attention, focused attention, speech, visuospatial and verbal working memory.

The present observed about 13% of children have frontal lobe function impairment.

**Jayashree et al. 1999**, observed impairment in attention, memory concentration & abstract thinking (24).

**Mitchell et al. 1991, Seidenberg et al. 1986**, also confirm the above using various Neuropsychological tests (8, 9).

**Thompson and Trimble et al. 1982** observed changes in reaction time, coding, attention, memory for faces in children with epilepsy (32).

## CONCLUSION

### To conclude

1. The prevalence of cognitive decline in school going epileptic children who are all on anti epileptic drugs is around 13%.
2. The cognitive function in them is adversely influenced by polytherapy. The relative risk of polytherapy vs Monotherapy is 4.69.
3. Longer duration of drugs (> 2 yr) found to significantly affect the cognitive function (along with polytherapy). There is 1.29 times risk of cognitive decline when antiepileptic drugs were taken for > 2 years duration.
4. Among the antiepileptic drugs phenobarbitone is found to have more affect over cognition.
5. Cogniive decline is less evident with valproate and carbamazepine.
6. Cognitive decline is found to be least affected with age group, sex, Literacy of Father and mother, Age at onset of seizures, Dosage, Type of Seizures.
7. Frontal lobe is affected in about 13.3%. Significant decline in motor speed, Attention, Verbal & Visuospatial working memory is noted. Speech is least affected.
8. Parietal lobe is affected in about 4.4%.
9. Temporal lobe is found to be not affected.

## **SUGGESTIONS**

1. Cognitive function assessment is a must for any children with epilepsy on antiepileptic drugs atleast for once in 6 months.
2. Avoidance of polytherapy at the most possible.
3. Avoidance of phenobarbitone ensures better outcome interms of cognition.

## PROFORMA

### EFFECT OF ANTIEPILEPTIC DRUGS ON COGNITIVE FUNCTIONS IN SCHOOL GOING CHILDREN WITH EPILEPSY

Name : OP No :

Age : S.No. :

Sex :

Education :

School :

Medium of Instruction :

School performance :  
(before antiepileptic drugs intake)

Father Education :

Mother Education :

Age at onset of Seizures :

Type of Seizure :

Drugs : Polytherapy / Monotherapy

Dosage :

Duration :

CT Scan Brain :

Date of assessment : 1

2

3

# NIMHANS NEUROPSYCHOLOGICAL BATTERY FOR CHILDREN

## 1. LFINGER TAPPING TEST

Trials	Number of Taps					Average no. of Taps
	1	2	3	4	5	
Right Hand	12	16	18	14	12	
Left Hand	10	15	14	16	10	

## 2. *HAND TAPPING TEST*

- |    |                                |           |
|----|--------------------------------|-----------|
| 1. | 2 right 1 left, 2 right 1 left | Fair/Poor |
| 2. | 3 right 2 left, 3 right 2 left | Fair/Poor |
| 3. | 2 left 3 right, 2 left 3 right | Fair/Poor |
| 4. | 3 left 2 right, 3 left 2 right | Fair/Poor |

## 3. TESTS FOR EXPRESSIVE SPEECH

### A. Repetitive Speech

- A.1 Repeating Sounds : ga, cha, ma, ra, sa, ha, ka, pa, na, sha.  
 .....

- A.2 Repeating Words : At, go; Sun, Cat; Train, Boat, Table, Plane, School, Pencil.

### B. Nominative Speech

- B.1. Object Naming : Naming five pictured objects.

- |      |                                     |                         |
|------|-------------------------------------|-------------------------|
| B.2. | One Word : Naming by Description    | <b>Correct Response</b> |
| i.   | What is it which tells time?        | Watch                   |
| ii.  | What is it which lays eggs?         | Hen                     |
| iii. | What is which protects from rain?   | Umbrella /Raincoat      |
| iv.  | What is it which has three colors?  | National Flag           |
| v.   | What is it which rules the country? | Government              |

### B.3. Categorical Naming

- |       |                                       |            |
|-------|---------------------------------------|------------|
| vi.   | Lion, Tiger, Fox Elephant             | Animals    |
| vii.  | Apple, Banana, Mango, Orange          | Fruits     |
| viii. | Carrot, Cabbage, Cauliflower, Raddish | Vegetables |
| ix.   | Bed, Table, Chair, Sofa               | Furniture  |

- |       |                                 |            |
|-------|---------------------------------|------------|
| x.    | Teacher, bag, books, uniform    | School     |
| xi.   | Mother, Father, Brother, Sister | Family     |
| xii.  | Cake, Candles, Gifts, Sweets    | Birthday   |
| xiii. | Paper, Pen, Pencil, Eraser      | Stationary |
| xiv.  | Axe, Hammer, Screwdriver, Screw | Tools      |
| xv.   | Gun, Pistol, Sword, Knife       | Weapons    |

### ***Narrative Speech***

#### Sentence Construction

1. Lion, Tiger, Zoo :.....
2. Ball, River, Play:.....
3. Picnic, Friends, Games:.....

Total Score :.....

#### **4. COLOR CANCELLATION TEST**

Time in Seconds :.....  
 Number of Omissions:.....  
 Number of Commissions.....

#### **10. COLOR TRAILS TEST**

	Time	Errors
Trail A		
Trail B		

#### **Qualitative Scores**

- i. Number of Errors :.....
- ii. Near misses :.....
- iii. Corrections:.....
- iv. Prompts:.....

6. **N BACK TASK, (VERBAL) FOR VERBAL WORKING MEMORY**

***List of Phonemes***

1 Back			2 Back		
Ga	<u>Ta</u>	Na	Dha	Pa	Na
Ja	Cha	Ga	Ba	Sa	Ka
Ja	Ra	<u>Na</u>	<u>Dha</u>	<u>Pa</u>	La
Cha	VA	Ma	Va	Ra	Dha
Ksha	VA	<u>Na</u>	Sha	<u>Pa</u>	Cha
<u>Ksha</u>	GA	Ma	<u>Va</u>	<u>Ra</u>	<u>Dha</u>
Ra	Da	Ka	Ga	Sa	<u>Cha</u>
Na	<u>Da</u>	<u>Ma</u>	Da	TA	Sa
Ma	RA	<u>Ka</u>	Na	Da	La
<u>Ma</u>	Na	La	<u>Da</u>	TA	
Ka	Sha	Tha	Cha	La	
Pa	<u>Sha</u>	Ja	Ra	Ha	
<u>Pa</u>	Ga	Ya	Sha	Va	
La	Va	<u>Ja</u>	Ja	<u>Ha</u>	
Va	<u>Va</u>	<u>Va</u>	<u>Sha</u>	JA	
Ta					

Note : The underlined items are the target responses (Hits).

Score	1 Back	2 Back
Hits		
Misses		



7. **N BACK TASK (VISUAL) FOR VISUOSPATIAL WORKING MEMORY**

1 Back				2 Back			
Sl.No.	Location of the dot	Sl.No.	Location of the dot	Sl.No.	Location of the dot	Sl.No.	Location of the dot
1.	5	19.	8	1.	4	19.	7
2.	8	20.	6	2.	5	20.	7
3.	9	21.	7	3.	3	21.	6
4.	7	22.	7	4.	5	22.	8
5.	7	23.	9	5.	4	23.	6
6.	5	24.	9	6.	1	24.	4
7.	4	25.	7	7.	3	25.	1
8.	4	26.	6	8.	2	26.	3
9.	2	27.	6	9.	3	27.	2
10.	2	28.	4	10.	5	28.	3
11.	3	29.	1	11.	6	29.	4
12.	1	30.	3	12.	7	30.	6
13.	5	31.	3	13.	8	31.	5
14.	5	32.	4	14.	7	32.	4
15.	6	33.	2	15.	9	33.	3
16.	8	34.	1	16.	6	34.	4
17.	8	35.	1	17.	8	35.	6
18.	9	36.	6	18.	9	36.	5

Note : Serial numbers represent the serial arrangement of cards and sequence of presentation. The underlined items and the underlined numbers representing the location of the dots are the target items.

**Scoring**

Score	1 Back	2 Back
Hits		
Misses		

8. **MOTOR-FREE VISUAL PERCEPTION TEST**

# SET – A

SET A (5-8 Years)					
Sl.No.	Correct Response	Response	Sl.No.	Correct Response	Response
1.	D		19.	A	
2.	A		20.	B	
3.	C		21.	C	
4.	C		22.	B	
5.	D		23.	A	
6.	B		24.	B	
7.	B		25.	D	
8.	D		26.	B	
9.	B		27.	D	
10.	B		28.	A	
11.	B		29.	A	
12.	D		30.	C	
13.	A		31.	D	
14.	D		32.	A	
15.	B		33.	B	
16.	D		34.	C	
17.	A		35.	C	
18.	A		36.	B	

## Motor Free Visual Perception Test : SET-B

SET A (9-12 Years)					
Sl.No.	Correct Response	Response	Sl.No.	Correct Response	Response
1.	A		19.	C	
2.	C		20.	B	
3.	A		21.	C	
4.	C		22.	B	
5.	B		23.	D	
6.	B		24.	A	
7.	C		25.	C	
8.	A		26.	B	
9.	A		27.	D	
10.	A		28.	C	
11.	C		29.	B	
12.	D		30.	A	
13.	B		31.	B	
14.	A		32.	B	
15.	C		33.	B	
16.	A		34.	D	
17.	D		35.	B	
18.	C		36.	C	

## 9. PICTURE COMPLETION TEST

Sl.No.	Items	Response	Sl.No.	Items	Response
1	Comb		11	Screw	
2	Table		12	Fly	
3	Cat		13	Rooster	
4	Fox		14	Profile	
5	Face		15	Watch	
6	Door		16	Umbrella	
7	Hand		17	Thermometer	
8	Card		18	House	
9	Fish		19	Cow	
10	Scissor		20	Flute	

Score : Number Correct : .....

## 10. READING, WRITING, CALCULATION

Reading a Passage

Errors :      Ignores Punctuation  
                 Adds letters  
                 Adds words  
                 Substitutes letters / words

Writing to Dictation : Number of words correct :

Copying :      Errors of substitution of letters, adding words or letters, letter reversals.

Calculation: Number correct :

## 11. TOKEN TEST

<b>A. Present only large tokens</b>	
1. Touch a circle	
2. Touch a square	
3. Touch a yellow token	
4. Touch a red token	
5. Touch a green token	
6. Touch a blue token	
7. Touch a white token	

Total =

<b>B. Present only large tokens</b>	
8. Touch the yellow square	
9. Touch the blue circle	
10. Touch the green circle	
11. Touch the white square	

Total =

<b>C. Present all tokens</b>	
12. Touch the small yellow circle	
13. Touch the large white square	
14. Touch the large blue square	
15. Touch the small green circle	

Total =

<b>D. Present large tokens only</b>	
16. Touch the red circle and yellow square	
17. Touch the blue square and white square	
18. Touch the green square and blue circle	
19. Touch the white circle and blue circle	

Total =

<b>E. Present all tokens</b>	
20. Touch the large white square and large red circle	
21. Touch the small yellow circle and large green square	
22. Touch the large blue square and large red square	
23. Touch the small white square and large red square	

Total =

<b>F. Present large tokens only</b>	
24. Put the red circle on the green square	
25. Touch the blue circle with the red square	
26. Touch the blue circle and the red square	
27. Pick up the blue circle OR the red square	
28. Put the green square away from the yellow square	
29. If there is a black circle, pick up the red square	
30. Put the green square beside the red circle	
31. Touch the squares slowly and the circles quickly	
32. Put the red circle between the yellow square and green square	
33. Except for the green one, touch all the circles	
34. Pick up the red circle – not the white square	

35.	Instead of the white square, take the yellow circle	
36.	Together with the yellow circle, take the blue circle	
Total =		

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## NORMATIVE PERCENTILES FOR EACH TEST

### 1. Normative Percentiles for Finger Tapping Test (Right hand)

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Motor speed (Right hand)	Finger tapping test (Right hand)	5	25	25	26	35	29	32	34
		6	26	26	27	31	35	34	36
		7	27	28	29	33	35	36	38
		8	28	29	30	35	35	38	39
		9	29	30	31	36	37	39	42
		10	31	31	33	37	39	42	43
		11	32	32	34	37	40	43	45
		12	33	33	35	37	41	45	47

### 2. Normative Percentiles for Finger Tapping Test (Left hand)

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Motor speed (Left hand)	Finger tapping test (Left hand)	5	22	23	24	25	27	29	31
		6	23	24	25	27	29	31	33
		7	24	25	26	28	28	33	34
		8	25	26	28	29	31	34	36
		9	27	28	30	33	35	37	39
		10	27	28	30	33	35	37	39
		11	28	29	31	34	36	39	40
		12	28	30	33	35	38	40	42

### 3. Normative Percentiles for Colour Cancellation Test

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Sustained Attention	Colour cancellation test (time in seconds)	5	23	25	27	29	31	32	33
		6	23	26	29	31	33	33	34
		7	24	27	29	31	33	34	35
		8	25	28	30	32	33	34	35
		9	26	29	31	32	34	34	35
		10	27	29	31	33	34	34	35
		11	28	30	31	33	34	35	35
		12	28	30	31	33	34	35	35

#### 4. Normative Percentiles for Colour Trails Test - Trail `A'

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Focused attention	Colour trails test `A' (Time in seconds)	8	63	76	94	108	146	166	197
		9	58	69	86	99	131	150	178
		10	54	64	78	92	118	137	161
		11	49	58	71	85	106	125	146
		12	46	54	64	78	95	113	132

#### 5. Normative Percentiles for Colour Trails Test - Trial `B'

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Focused Attention	Colour Trials Test `B' (time in seconds)	8	138	153	187	225	264	296	326
		9	125	136	169	203	239	269	295
		10	114	122	154	184	215	244	266
		11	104	109	140	166	194	222	240
		12	94	98	127	149	175	202	217

#### 6. Normative Percentiles for N back task (Verbal) - 1 back

			Percentile points			
Function	Tests	Age	5	10	25	50
Verbal working memory	N back Test 1 back	5	5	6	7	8
		6	6	7	7	8
		7	7	7	8	9
		8	7	8	8	9
		9	8	8	9	9
		10	8	8	9	9
		11	8	8	9	9
		12	8	8	9	9

## 7. Normative Percentiles for N back task (Verbal) - 2 back

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Verbal working memory	N back test 2 back	5	7	8	9	11	13	14	15
		6	7	9	10	12	13	15	17
		7	8	10	11	13	14	16	17
		8	9	10	11	13	15	17	18
		9	10	11	12	14	15	18	19
		10	11	12	13	15	16	18	19
		11	11	12	13	15	17	18	19
		12	12	12	14	16	17	19	19

## 8. Normative Percentiles for N back task (visual) - 1 back

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Visuospatial working memory	N back test 1 back (Hits)	5	4	5	6	7	8	8	9
		6	5	6	6	7	9	9	9
		7	5	6	6	7	9	9	10
		8	6	7	7	8	9	10	10
		9	6	7	7	8	10	10	10
		10	6	7	7	8	10	10	10
		11	7	8	8	9	10	10	10
		12	7	8	8	9	10	10	10

## 9. Normative Percentiles for N back task (visual) - 2 back

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Visuospatial working memory	N back test 2 back (Hits)	5	1	1	1	1	2	2	3
		6	1	1	1	2	2	3	3
		7	1	1	1	2	3	3	4
		8	1	1	2	3	3	4	4
		9	1	1	2	3	4	4	5
		10	1	2	2	3	4	5	5
		11	1	2	3	3	4	5	5
		12	1	2	3	3	4	5	5

### 10. Normative Percentiles for Motor - Free Visual Perception Test

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Visuospatial working memory	MVPT	5	20	21	24	25	27	29	30
		6	21	23	25	27	29	31	32
		7	22	24	25	28	29	32	33
		8	23	25	26	29	30	33	33
		9	23	26	27	29	31	33	34
		10	24	26	28	30	32	33	34
		11	25	27	28	31	32	33	34
		12	25	27	29	31	32	33	34

### 11. Normative Percentiles for Picture Completion Test

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Visual memory	Picture completion	5	5	5	7	8	9	10	11
		6	5	6	7	8	9	10	11
		7	5	6	7	8	10	10	11
		8	5	6	8	9	10	11	12
		9	5	7	8	9	10	11	12
		10	5	7	8	10	11	12	13
		11	5	8	9	10	11	12	13
		12	5	8	9	10	11	13	14

### 12. Normative Percentiles for Token Test

			Percentile points						
Function	Tests	Age	5	10	25	50	75	90	95
Verbal comprehension	Token test	5	23	25	27	29	31	32	33
		6	23	26	29	31	33	33	34
		7	24	27	29	31	33	34	35
		8	25	28	30	32	33	34	35
		9	26	29	31	32	34	34	35
		10	27	29	31	33	34	34	35
		11	28	30	31	33	34	35	35
		12	28	30	31	33	34	35	35

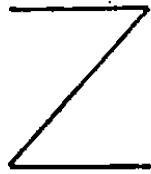
## KEY TO MASTER CHART

Age	-	7 to 9 years - 1 10 - 12 years - 2
Sex	-	Male - 1 Female - 2
Father Education	-	Literate - 1 Illiterate - 2
Mother Education	-	Literate - 1 Illiterate - 2
Age at Onset of Seizures	-	Below 6 years - 1 above 6 years - 2
Type of Seizures	-	GTCS - 1 Focal - 2 CPS - 3 SPS - 4
Type of therapy	-	Monotherapy - 1 Polytherapy - 2
Duration of Drugs	-	1 - 2 years - 1 2 - 4 years - 2 4 - 6 years - 3
PBT	-	Yes - 1 No - 2
PHT	-	Yes - 1 No - 2
SVP	-	Yes - 1 No - 2
CBZ	-	Yes - 1 No - 2
Dosage	-	Yes = usual Dose = 1 No = Higher Dose = 2

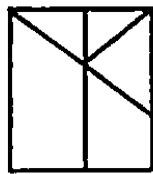
## ABBREVIATIONS

AG-SZ	-	Age at onset of seizures
TY-SZ	-	Type of seizures
GTCS	-	Generalised tonic clonic seizures
CPS	-	Complex partial seizures
SPS	-	Simple partial seizures
PBT	-	Phenobarbitone
PHT	-	Phenytoin
CBZ	-	Carbamazepine
SVP	-	Sodium valproate
FTT	-	Finger tapping test
R/L	-	Right / Left
HT	-	Hand tapping test
CCT	-	Color cancellation test
CTA	-	Color trail test A
CTB	-	Color trail test B
SPSC	-	Speech score
NBT <sub>1</sub>	-	N Back test <sub>1</sub>
NBT <sub>2</sub>	-	N Back test <sub>2</sub>
VSNBT <sub>1</sub>	-	Visuospatial N Back test <sub>1</sub>
VSNBT <sub>2</sub>	-	Visuospatial N Back test <sub>2</sub>

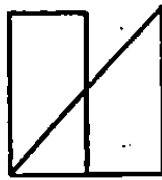
# MOTOR - FREE VISUAL PERCEPTION TEST (MVPT) SAMPLE CARD



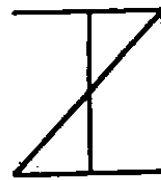
A



B

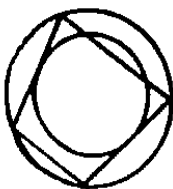
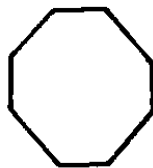


C

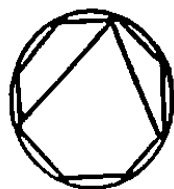


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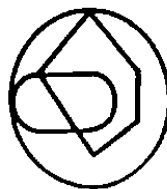
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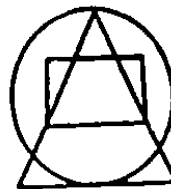
A



B



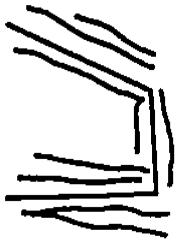
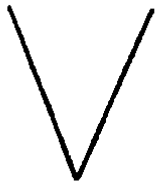
C



D



**MOTOR - FREE VISUAL PERCEPTION  
TEST (MVPT) SAMPLE CARD**



A



B



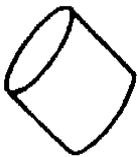
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D

12

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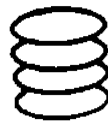
A



B



C



D